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10/552,155	01/12/2006	Martin Laforest	701826-57350	9212
7590 David S Resnick Nixon Peabody 100 Summer Street Boston, MA 02110			EXAMINER WILDER, CYNTHIA B	
			ART UNIT	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/552,155

**Applicant(s)**

LAFOREST ET AL.

**Examiner**

CYNTHIA B. WILDER

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 32-34 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-31, 35, 36, 38 and 39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10/11/2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/19/2008.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Applicant's amendment filed 12/19/2008 is acknowledged and has been entered. Claims 1, 18, 21, 22, 24 and 27 have been amended. Claims 1-39 are pending. Claims 32-34 and 37 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-31, 35-36, 38 and 39 are discussed in this Office action. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

**This action is made FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Previous Rejection***

3. The prior art rejections under 35 USC 103(a) as being unpatentable over Antonarakis et al are withdrawn in view of Applicant's amendment of the claims. The prior art rejections under 35 USC 103(a) as being unpatentable over Antonarakis et al in view of Pourmand et al are withdrawn in view of Applicant's amendment.

#### ***New Ground(s) of Rejections***

**THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:**

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

***Claim Interpretation***

The specification does not provide a specific definition of the term "sequential dispensation order of individual nucleotides", but implies throughout the specification that the term is in reference to primer extension by "pyrosequencing". Accordingly, for the purpose of application of prior art, the limitations of the "wherein clause" of the claims 1, 18, 22 and 24 is being interpreted by the examiner as performing steps of "pyrosequencing" of a target and control nucleic acid to obtain the desired information. With regards to the limitation wherein said coamplifying is stopped during an exponential phase, the limitation is being interpreted by the examiner as submaximal

amplification conditions or wherein the exponential phase has been stopped or wherein an amplification plateau has not been reached.

***Claim Rejections - 35 USC § 103***

The following are new grounds of rejections necessitated by Applicant's amendments. Although the claims were previously rejected as being unpatentable over Antonarakis et al, Applicant's amendments have necessitated the inclusion of new grounds of rejections in the present rejection. It is noted that, to the extent that Antonarakis et al apply to the present rejection; Applicant's arguments are addressed following the rejection.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-9, 15-26, 35-36, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antonarakis et al (US 20030054386 A1, effective filing date June 2001) in view of Ryder et al (5705365, January 1998). Regarding claims 1, 18, 22 and 24, Antonarakis et al teach a method comprising: a) co-amplifying a target nucleic acid sequence and a known amount of a known control nucleic acid sequence to produce respective target and control amplicons 0012-0014, 0049), wherein said control nucleic acid sequence is different than said target nucleic acid sequence (0049); and b) determining relative amounts of said respective amplicons by determining relative quantities of a primer extension reaction using each of said respective amplicons as a template, wherein said primer extension reaction is performed using steps of pyrosequencing (0014) and wherein determining relative quantities of a primer extension reaction comprises comparing a quantity of nucleotides incorporated during said primer extension reaction for said target amplicon with a quantity of nucleotides incorporated during said primer extension reaction for said control amplicon, wherein relative amounts of said respective amplicons are proportional to relative quantities of nucleotides incorporated during said primer extension reactions and said amount of said target nucleic acid sequence in said sample is proportional thereto (0078-0090). Antonarakis et al teach that the method allows detection of the relative dose of a target as compared to a known control (0049) and allows the identification of a desired target (0011). With regards to assessing copy number, Antonarakis et al recognizes the problems of prior hybridization-based methods in determining copy number. Antonarakis et al teach at paragraph 0009:

"[I]n CGH analysis, test samples comprising labeled genomic DNA containing an unknown dose of a target genomic region and control samples comprising labeled genomic DNA containing a known dose of the target genomic region are applied to an immobilized genomic template and hybridization signals produced by the test sample and control sample are compared. The ratio of signals observed in test and control samples provides a measure of the copy number of the target in the genome. Although CGH offers the possibility of high throughput analysis, the method is difficult to implement since normalization between the test and control sample is critical and the sensitivity of the method is not optimal."

Antonarakis et al disclose that the method solves the problem of the prior art (see 0011). Likewise Antonarakis teaches the advantages of performing primer extension by pyrosequencing. Antonarakis et al teach "using a pyrosequencing, 96 samples can be analyzed simultaneously in less than 30 minutes". Antonarakis et al teach that "[T]he analysis does not require gel electrophoresis or any further sample processing since the output from the Pyrosequencer provides a direct quantitative ratio enabling the user to infer the genotype and hence phenotype of the individual from whom the sample is obtained. By using a paralogous gene as a natural internal control, the amount of variability from sample handling is reduced. Further, no radioactivity or labeling is required (0086).

Antonarakis et al do not expressly teach wherein the coamplifying is stopped during an exponential phase of the coamplification.

Ryder et al teach a method of detecting a target by amplification, the method comprising coamplification of multiple nucleic acid sequences and multiple primer pairs in a multiplex format. Ryder teaches wherein in a coamplifying step, the reaction plateau is not reach. (See col. 7, line 48 to col. 8, line 20, which teaches that the amplification is performed in submaximal conditions, which is meant that the reaction

conditions are altered from those yielding the greatest amount of product for a given target and primer combination; see also col. 9, line 55 to col. 10, line 42). Ryder teaches that amplification under submaximal conditions results in a reproducible correlation between target input levels and target specific product levels when amplification is conducted under defined conditions. Ryder further teaches that a suboptimal amplification can allow for accurate detection of higher initial target levels without resort to dilution of the product samples (col. 8). In view of the foregoing, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to perform the amplification reaction wherein the reaction has not reached plateau for the benefit of allowing for the accurate detection of higher initial target levels without resorting to dilution of the product sample as suggested by Ryder et al.

Regarding claims 2, 19, 23 and 26, Antonarakis et al teach wherein said control nucleic acid is an endogenous nucleic acid (0086).

Regarding claims 3 and 11, Antonarakis et al teach wherein said primer extension reaction is performed using identical primers for said respective target and control amplicons (0093).

Regarding claim 4, Antonarakis et al teach wherein said primer extension can be performed using different primer pairs for each set of genes (0049).

Regarding claim 5, Antonarakis et al teach wherein said primer extension reaction is detected by detecting pyrophosphate (PPi) release (0084).



Regarding claim 6, Antonarakis et al teach wherein said pyrophosphate is detected luminometrically (0084).

Regarding claim 7, Antonarakis et al teach wherein said pyrophosphate is detected enzymatically using the enzyme luciferase as a PPI-detection enzyme (0084).

Regarding claim 8, Antonarakis et al teach wherein in the primer extension reaction, an alpha-thio analogue of an adenine nucleotide is used (0084).

Regarding claim 9, Antonarakis et al teach wherein said target nucleic acid and control nucleic acid are co-amplified using amplification primers which are immobilized or carry means for immobilization (0081).

Regarding claims 15, Antonarakis et al teach wherein each primer extension reaction yields an extension product of different lengths or sequences (0078).

Regarding claim 16, 17, 20, 21, 27, Antonarakis et al teach wherein the target nucleic acid is a gene or a fragment of a gene conferring an investigated trait (see 0014-0030 and Table 1).

Regarding claims 28-30, Antonarakis et al teach wherein the target organism is a mammalian organism, such as human (see examples at pages 10-11).

Regarding claims 31, and 35-36, 38 and 39, Antonarakis et al teach wherein the target nucleic acid is a chromosome (see Table 1 and Abstract and Examples). Antonarakis et al do not teach wherein the target or control is an enzyme as recited in the claims 31 and 35, 36, 38 and 39. However, the claims recite a plethora of conventional nucleic acid manipulation reagents and methodologies based on the

practitioner's desired results, as well as well as routine optimization of reaction components and parameters based on the practitioner's desired results. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications based on the practitioner desired results. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using any desired target or control nucleic acid based on the practitioner's desired results.

9. Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antonarakis et al in view of Ryder et al as previously applied above and further in view of Pourmand et al (Nucleic acids Research, vol. 30, no. 7, pages e31, 2002). Regarding claim 10-14, Antonarakis et al in view of Ryder et al teach the use of multiple control and target sequences that can be analyzed by the pyrosequencing methodology (see for example table 1 and 0068 and examples. Antonarakis et al teach that 96 well can be used to perform the pyrosequencing method. Further methods of multiplex pyrosequencing in a single reaction vessel are known in the art. For example, Pourmand et al teach a multiplex pyrosequencing method. Pourmand et al teach that the method is useful because is rapid, efficient and very accurate (see discussion at pages 3, col. 2 to col. 1 of page 4). One of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the quantitative method of Antonarakis et al in view of Ryder et al to encompass performing a multiplex pyrosequencing method for multiple controls and target nucleic acids based on the

advantages taught by Pourmand et al that multiplex pyrosequencing is rapid, efficient and very accurate. It would be *prima facie* obvious to one of ordinary skill in the art that predictable results can be obtained in determining a target or assessing copy number as suggested by Pourmand et al.

10. Claims 1-9, 15-26, 35-36, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antonarakis et al (citation made of record in prior Office action) in view Haemmerle et al (5858658, January 1999). Regarding claims 1, 18, 22 and 24, Antonarakis et al teach a method comprising: a) co-amplifying a target nucleic acid sequence and a known amount of a known control nucleic acid sequence to produce respective target and control amplicons 0012-0014, 0049), wherein said control nucleic acid sequence is different than said target nucleic acid sequence (0049); and b) determining relative amounts of said respective amplicons by determining relative quantities of a primer extension reaction using each of said respective amplicons as a template, wherein said primer extension reaction is performed using steps of pyrosequencing (0014) and wherein determining relative quantities of a primer extension reaction comprises comparing a quantity of nucleotides incorporated during said primer extension reaction for said target amplicon with a quantity of nucleotides incorporated during said primer extension reaction for said control amplicon, wherein relative amounts of said respective amplicons are proportional to relative quantities of nucleotides incorporated during said primer extension reactions and said amount of said

target nucleic acid sequence in said sample is proportional thereto (0078-0090). Antonarakis et al teach that the method allows detection of the relative dose of a target as compared to a known control (0049) and allows the identification of a desired target (0011). With regards to assessing copy number, Antonarakis et al recognizes the problems of prior hybridization-based methods in determining copy number. Antonarakis et al teach at paragraph 0009:

"[I]n CGH analysis, test samples comprising labeled genomic DNA containing an unknown dose of a target genomic region and control samples comprising labeled genomic DNA containing a known dose of the target genomic region are applied to an immobilized genomic template and hybridization signals produced by the test sample and control sample are compared. The ratio of signals observed in test and control samples provides a measure of the copy number of the target in the genome. Although CGH offers the possibility of high throughput analysis, the method is difficult to implement since normalization between the test and control sample is critical and the sensitivity of the method is not optimal."

Antonarakis et al disclose that the method solves the problem of the prior art (see 0011). Likewise Antonarakis teaches the advantages of performing primer extension by pyrosequencing. Antonarakis et al teach "using a pyrosequencing, 96 samples can be analyzed simultaneously in less than 30 minutes". Antonarakis et al teach that "[T]he analysis does not require gel electrophoresis or any further sample processing since the output from the Pyrosequencer provides a direct quantitative ratio enabling the user to infer the genotype and hence phenotype of the individual from whom the sample is obtained. By using a paralogous gene as a natural internal control, the amount of variability from sample handling is reduced. Further, no radioactivity or labeling is required (0086).

Antonarakis et al do not expressly teach wherein the coamplifying is stopped during an exponential phase of the coamplification.

Haemmerle et al teach a method of quantitating genomic DNA, the method comprising adding in the sample a given amount of at least one nucleic acid as a control wherein the control differs from the genomic DNA to be quantified in at least one detectable characteristic, and the amount of amplified genomic DNA and the amount of control are determined and departing from the amount of control obtained, the amount of the genomic DNA originally present in the sample is determined (abstract and col. 2, lines 46-57). Haemmerle et al teach that various known concentrations of a genomic DNA of a species are amplified with the methods according to the invention in a competitive nucleic acid amplification method by using a control. Haemmerle et al is stopped in the exponential phase, and the amounts of the amplified nucleic acids are determined (col. 4, lines 33-37). Haemmerle et al teach that the reproducibility of the method according to the invention amounts in at least 95%. Haemmerle et al teach to obtain this, care must be taken that the efficiency of the amplification reaction for the control and the sample is equal. Haemmerle teach that the efficiency of the amplification reaction is primarily of importance if it is stopped in the exponential phase (col. 5, lines 41-46). Haemmerle et al teach that besides high sensitivity and particularly low detection limit of the method, new quality criteria can be determined for biological products which are defined by an extremely low or absent content of contaminating nucleic acids (col. 45. 57-61).

In view of the foregoing, one of ordinary skill in the art at the time of the claimed invention, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the quantitation method of Antonarakis et al to encompass a step wherein the co-amplification is stopped during an exponential phase of the coamplification as taught by Haemmerle et al for the obvious benefit of increasing efficiency of the reaction thus more accurately determining the amount of genomic DNA in a sample as suggested by Haemmerle.

Regarding claims 2, 19, 23 and 26, Antonarakis et al teach wherein said control nucleic acid is an endogenous nucleic acid (0086).

Regarding claims 3 and 11, Antonarakis et al teach wherein said primer extension reaction is performed using identical primers for said respective target and control amplicons (0093).

Regarding claim 4, Antonarakis et al teach wherein said primer extension can be performed using different primer pairs for each set of genes (0049).

Regarding claim 5, Antonarakis et al teach wherein said primer extension reaction is detected by detecting pyrophosphate (PPi) release (0084).

Regarding claim 6, Antonarakis et al teach wherein said pyrophosphate is detected luminometrically (0084).

Regarding claim 7, Antonarakis et al teach wherein said pyrophosphate is detected enzymatically using the enzyme luciferase as a PPi-detection enzyme (0084).

Regarding claim 8, Antonarakis et al teach wherein in the primer extension reaction, an alpha-thio analogue of an adenine nucleotide is used (0084).

Regarding claim 9, Antonarakis et al teach wherein said target nucleic acid and control nucleic acid are co-amplified using amplification primers which are immobilized or carry means for immobilization (0081).

Regarding claims 15, Antonarakis et al teach wherein each primer extension reaction yields an extension product of different lengths or sequences (0078).

Regarding claim 16, 17, 20, 21, 27, Antonarakis et al teach wherein the target nucleic acid is a gene or a fragment of a gene conferring an investigated trait (see 0014-0030 and Table 1).

Regarding claims 28-30, Antonarakis et al teach wherein the target organism is a mammalian organism, such as human (see examples at pages 10-11).

Regarding claims 31, and 35-36, 38 and 39, Antonarakis et al teach wherein the target nucleic acid is a chromosome (see Table 1 and Abstract and Examples). Antonarakis et al do not teach wherein the target or control is an enzyme as recited in the claims 31 and 35, 36, 38 and 39. However, the claims recite a plethora of conventional nucleic acid manipulation reagents and methodologies based on the practitioner's desired results, as well as well as routine optimization of reaction components and parameters based on the practitioner's desired results. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications based on the practitioner desired results. It would have been

*prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using any desired target or control nucleic acid based on the practitioner's desired results.

11. Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antonarakis et al in view Haemmerle et al as previously applied above and further in view of Pourmand et al (Nucleic acids Research, vol. 30, no. 7, pages e31, 2002). Regarding claim 10-14, Antonarakis et al in view Haemmerle et al teach the use of multiple control and target sequences that can be analyzed by the pyrosequencing methodology (see for example table 1 and 0068 and examples. Antonarakis et al teach that 96 well can be used to perform the pyrosequencing method. Further methods of multiplex pyrosequencing in a single reaction vessel are known in the art. For example, Pourmand et al teach a multiplex pyrosequencing method. Pourmand et al teach that the method is useful because is rapid, efficient and very accurate (see discussion at pages 3, col. 2 to col. 1 of page 4). One of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the quantitative method of Antonarakis et al in view of Haemmerle et al to encompass performing a multiplex pyrosequencing method for multiple controls and target nucleic acids based on the advantages taught by Pourmand et al that multiplex pyrosequencing is rapid, efficient and very accurate. It would be *prima facie* obvious to one of ordinary skill in the art that predictable results can be obtained in determining a target or assessing copy number as suggested by Pourmand et al.



***Response to Arguments***

12. Applicant traverses the prior art of Antonarakis et al on the following grounds: Applicant states that Antonorakis et al fails to teach to those of skill in the art that an unrelated control sequence be used. Applicant states that the claims are not limited to pyrosequencing processes. Applicant states Antonarakis does not teach that the coamplification must be stopped during the exponential phase of the coamplification. Applicant states that the method of the instant invention is not limited to the degree of identity between the target and control sequence, the method is not limited to amplification products that are similar on length or that have similar amplification efficiencies. With regards to Pourmand et al, Applicant states that the reference does not teach stopping the co-amplification step during the exponential phase of the amplification.

13. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response to Applicant's arguments concerning Antonorakis et al, it is noted that the claims are not limited to unrelated control sequences, the claims do exclude products having similar length or similar efficiencies, thus this argument is not found persuasive. MPEP states although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In response to Applicant's arguments concerning stopping coamplification during the exponential phase, it is noted that this limitation was not previously presented in the previously rejected claims, accordingly this argument is moot. In response to Applicant's

arguments that the claims are not limited to pyrosequencing, it is noted that the claims do not exclude pyrosequencing and further the instant specification supports the use of pyrosequencing (see Figure 3 and page 13 which teaches that Figure 3 illustrates pyrosequencing results). Applicant's arguments are not found persuasive to remove the Antonorakis et al.

### ***Conclusion***

14. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **CYNTHIA B. WILDER** whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/  
Supervisory Patent Examiner, Art Unit 1637